Biosciences, Biotechnology Research Asia Vol. **4**(1), 325-328 (2007)

Synthesis and biological screening of 2,5 -disubstituted 1,3,4 oxadiazole derivatives

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(Received: April 09, 2007; Accepted: May 12, 2007)

ABSTRACT

Synthesis of a number of 1,3,4 – oxadiazole derivatives have been described. Benztriazole reacting with ethylcholoro acetate in the presence of potassium carbonate to produce ethyl 2 – (1H benzo[d][1,2,3] triazol – 1 yl] acetate) which further react with hydrazine hydrate to produced (2H-benzo [d][123] triazole – 1 yl aceto hydrazide] and this react with different aromatic acid in presence of phosphorus oxychloriede offerda 2,5 disubstituted 1,3,4 oxadiazole derivatives. Compounds were tested for antibacterial and antifungal activity.

Key words: 1,3,4 – oxadiazole derivatives and antimicrobial activity.

INTRODUCTION

2, 5 – Disubstututed 1,3,4 – oxadiazole derivatives possesses as broad spectrum pharmacological activities such as antibacterial activity[1], antifungal[2], antimalarial[3], anticonvulsont[4], and anti-inflammatory[5] activities.

5- (benztriazole – 1yl – methyl) – 2 phenyl – 1,3,4 oxadiazole derivatives possesses antifungal and antibacterial activity[6].

Reaction between benzotriazole with ethyl chloro acetate in the presence of potassium carbonate produced ethyl – 2 (1 H benzo [d][1,2,3] triazole – 1 yl] acetate (step – 1) the product obtained from step – 1 react with hydrazine hydrate to produced (2 H – benzo [d] [1,2,3] triazole – 1 – yl acetohydrazide (step – 2) after this the product obtained from step – 2 react with different aromatic acids in the presence of phosphorus oxychloride produced different derivatives (G1 – G4).

MATERIAL AND METHODS

All the chemicals used were AR grade and some were LR grade, procured from various chemicals units like Merek, Mumbai, Qualigens, Mumbai, s.d.Fine, Mumbai and CDH – New Delhi. Melting points were determined in open glass capillaries and are uncorrected. The IR Spectra (KBr dise) were recorded on FTIR Perkin Elmer. ^{1}H NMR spectra were recoded in DMSO using Bruker Avance – II 400 NMR spectrophotometer. The chemical shifts were expressed in ä units in ppm downfield from TMS. The purity and completion of reaction was monitored by TLC using n hexane : benzene (1 : 2) solvent system and silica gel – G coated glass plates as solid support.

Synthetic study

Step – I

Preparation of ethyl 2- (1H benzo[d][1,2,3] triazol – 1 yl] acetate.

A mixture of equimolar quantity of benztriazole (0.01M) and ethyl chloro acetate (0.01 M) was added with stirring to acetone (60 ml) in presence of potassium carbonate for 6 hours.

The solvent was removed under reduced pressure and product was recrystalized with diethyl ether. The ether was remove under reduced pressure and get needle shaped brown crystal of compound S_1

Yield - 89 %
M.P. – 60°C

Step – II

Preparation of (2H – benzo[d][1,2,3] triazole – 1 yl aceto hydrazide]

Compound S_1 (0.01M) and hydrazine hydrate stirred in ethanol for 4 hours then refluxed on water both for 3 hours. The excess solvent was removed by distillation. The solid crystal of compound S_2 was obtained which is recrystalized with ethanol.

Yield – 80 %
M.P. – 120°C

Step – III

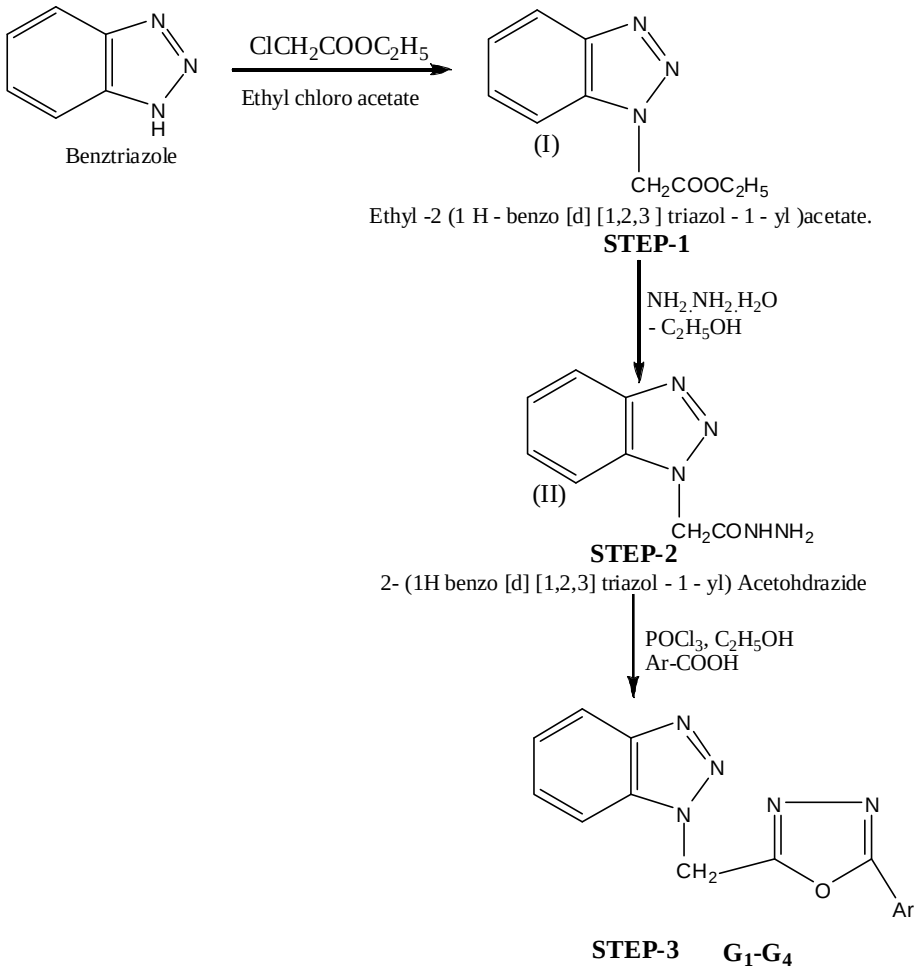
(Derivatives)

Compound S_2 (0.01 M) was reflux with different aromatic acids (0.01 M) in the presence of phosphorus oxychloride (10 ml) for 6 hours.

The content was poured in ice-cold water and alkaline with sodium bicarbonate. The separated solid was filtered and recrystalized with ethanol. Similarly other derivatives were also prepared by the same method.

Antimicrobial activity

The synthesized compound were tested for their antibacterial activity against *S. aureus,*



Reaction Scheme

E. coli, S.P.A and B. subtilis using agar cup method[7] at 40 µg/ml. The zone of inhibition with respect to controlled medium is given in Table -1. The sensitivity of the compound against the test microbes was compared with standard drug ciprofloxacin.

The synthesized compounds were also screened for their antifungal activity by using fusarium solani. The zone of inhibition were measured and the percentage inhibition was calculated. For standard Griseofulvin was used and percentage inhibition was 83%.

RESULTS AND DISCUSSION

From the experimental data it has been found that derivate G_1 and G_3 process no activity against S. aureus. The remaining derivatives are active against S. aureus. The derivative G_1 to G_4 so good activity against E.coli.

In case of gram negative bacteria like S.P.A. only G_3 show activity. Derivative G_3 are also active against B. subtilis bacteria. From the experimental data it was observed that the compound G_2 and G_3 showed considerable inhibition against Griseofulvin.

Table - 1: Antimicrobial activity

S. No.	Compound	Antifungal activity (% inhibition)	Antibacterial activity (zone of inhibition in mm)			
			S. aureus	*E.coli*	S.P.A	*B. subtilis*
1.	G_1	20	-	12	-	-
2.	G_2	50	9	12	-	-
3.	G_3	56	-	14	10	8
4.	G_4	-	12	10	-	-
Standard	Ciprofloxacin	-83	25-	24-	20-	22-
	Griseofulvin					

Table - 2 : Physical and Analitical Data of Compounds

S.No.	Compound	Ar - COOH	Molecular formula	m.p. (°C)	Yield %
1	G_1	p-Hydroxy benzoic acid	$C_{15}H_{11}N_5O_2$	185	49
2	G_2	p-nitro benzoic acid	$C_{15}H_{10}N_6O_3$	170	52
3.	G_3	3,5 – dintro salicylic acid	$C_{15}H_9N_7O_6$	178	50
4.	G_4	Iso-phthalic acid	$C_{22}H_{17}N_5O_2$	167	55

Table - 3 : IR, NMR Data of compounds

S.No.	Compound	IR	NMR
1.	G_1	Ar-C=C-1550 Ar-C-H-3050 Ar-C-N-1180 N=N - 1429 CH_2 - 2870 OH-3450 N-C-1240	CH_2-4.9(H,s) Ar(-OH) - 9.4 (1H,s) Benztriazole (C-H)-7.4 to 7.9 (4H,m) Bezene (C-H) 6.8 to 7.9 (4H,m)
2.	G_2	Ar-C=C-1550 Ar-C-H-3050 Ar-C-N-1180 N=N - 1429 N-C-1240 C-NO_2-1300	CH_2-4.9(H,s) Benztriazole (C-H)-7.4 to 7.9 (4H,m) Bezene (C-H) 8.2 to 8.3 (2H,d)
3.	G_3	Ar-C=C-1550 Ar-C-H-3050 Ar-C-N-1180 N=N - 1429 CH_2 - 2870 OH-3450 N-C-1240 C-NO_2-1300	CH_2-4.9(H,s) Ar-OH - 9.4 (1H,s) Benztriazole (C-H)-7.4 to 7.9 (4H,m) Bezene (C-H) 8.7 to 8.8 (2H,s)
4.	G_3	Ar-C=C-1550 Ar-C-H-3050 Ar-C-N-1180 N=N - 1429 CH_2 - 2870 OH-3450 N-C-1240	CH_2-4.9(H,s) C-OH - 6.8 (1H,s) Benztriazole (C-H)-7.4 to 7.9 (4H,m) Bezene (C-H) -7.3 (10H,m)

ACKNOWLEDGEMENTS

The authors are thankful to Dr. Raghuveer Irchhaiya (H.O.D.) Institute of Pharmacy Bundelkhand University, Jhansi,. providing various laboratory facilities and Dr. R.K. Agrawal (Microbiology Department Medical College Jhansi,) for arranging the screening of these compounds.

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